

Original article

Asthma definitions, relative validity and impact on known risk factors in young Brazilians

Background: An asthma score was proposed in the European Community Respiratory Health Survey (ECRHS) framework, as dichotomous definitions could be less appropriate in the study of chronic diseases. The aims of this study were to assess the value of this asthma score in comparison with other definitions of asthma in another population setting, using as criteria bronchial hyperresponsiveness (BHR) to methacholine and diagnosed asthma, and the association of these definitions to known risk factors of asthma.

Methods: We used the ECRHS questionnaire on 2063 Brazilians, aged 23–25 years, and measured their BHR. We assessed the positive and negative likelihood ratios (PLR and NLR) of the asthma score (0–8), a three question score (ECRHS definition) and single asthma symptoms in relation to BHR and diagnosed asthma.

Results: The PLR were relatively low for all asthma definitions with odd ratios varying from 1.47 for asthma score to 5.50 for wheeze and waking with breathlessness without a cold. The NLR were near 1. The PLR were lower for assessments using the score than for dichotomous assessments or the ECRHS definition. The PLR increased with asthma scores, but the prevalence with higher scores was too low for useful analysis. The asthma score was slightly better for identifying associations from a set of known risk factors than the other two approaches.

Conclusion: Our study provided little support for a greater validity of this asthma score over other asthma definitions, and only marginal advantage for identifying risk factors.

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The study of the aetiology of asthma has been hampered by lack of consistency in the results between reports. Most definitions of asthma emphasize variable airflow obstruction and highlight inflammation as essential elements of the condition (1, 2). These characteristics do not translate into an unambiguous definition to separate asthmatics and nonasthmatics in surveys (3). The European Community Respiratory Health Survey (ECRHS) and the International Study of Asthma and Allergy in Childhood (ISAAC) contributed to the study of asthma by developing standardized questionnaires of asthma (4, 5). The common approach of using a single subjective symptom, however, has not provided a clear diagnosis of asthma, and the use of dichotomous outcomes for assessing risk factors leads to a reduction of statistical power.

The uncertainty of the validity of the outcomes used is difficult to disentangle because there is evidence that asthma symptoms, following a demonstration of these symptoms, do not show a greater agreement with bronchial hyperresponsiveness (BHR) to methacholine

in comparison with answers from participants who have not received such explanations (6). The prevalence of asthma, using participant responses in a survey and clinical judgement by a panel of chest clinicians, was similar regardless of method (7), but others reported disagreement between paediatricians in relation to the severity and the clinical diagnosis of asthma based on a set of vignettes (8).

As asthma is a chronic disease, we should be cautious in relying on dichotomous variable to study its aetiology. Pekkanen et al. (1) evaluated the use of continuous asthma scores, using data from 34 ECRHS centres based on eight questions. Their results were inconclusive in so far as they found that dichotomous definitions of asthma had higher odds ratios (OR), but symptoms of asthma are possibly best analysed as a continuous asthma score because that does not rely on a threshold value (1).

We have carried out a survey in young Brazilians using the ECRHS questionnaire, and assessing atopy to eight allergens and BHR to methacholine. The aim of this study was to assess the relative validity of a continuous score of

asthma as suggested by Pekkanen et al. (1), single asthma symptoms, and the ECRHS definition of asthma using three questions, in relation to a positive BHR to methacholine, positive BHR and atopy, and physician diagnosed asthma. We also assessed these three asthma definitions in relation to known risk factors of asthma (1).

Methods

Of the total cohort, 6973 livebirth, 5665 subjects were singleton, alive by the age of 20 years, living in Ribeirão Preto, São Paulo state, for whom current addresses were available using multiple electronic sources (9). This study was based on 2063 men and women aged 23–25 years selected from a cohort of babies born from 1 June 1978 to 31 May 1979. This sample size was calculated to assess at a 5% significance level, the difference of proportions of 12% with a power of 80% when the overall prevalence of an event was 10%. This prevalence is appropriate for the great majority of the respiratory symptoms in Brazil.

We selected the sample as follows: the 5665 individuals were located initially via fixed or mobile phones, as telephones are very common in Ribeirão Preto. We also sent letters explaining the study, a contact telephone, and publicized the study in the media and through posters in health services. We divided the city into four geo-economic areas by income of the head of the family: 'poor', 'middle-poor', 'middle-wealthy' and 'wealthy' (10). A third of the individuals in each area were invited to participate. Of the selected individuals, 705 were replaced because of their refusal to participate (209 subjects), death after the age of 20 years (34 subjects), custodial sentence (31 cases) and failure to attend the interview (431 subjects).

The number of inhabitants of Ribeirão Preto is approximately 550 000 and the main economic activities are the sugarcane industry, trading, services and banking. Data collection was performed between 2002 and 2004. Further information is available elsewhere (9). The study was approved by the Ethics Committee of the University Hospital, Medical School of Ribeirão Preto.

Respiratory questionnaire

Respiratory symptoms were assessed using the ECRHS questionnaire translated into Portuguese and adapted to the Brazilian lexicon. The symptoms used in this analysis were wheezing or whistling in the chest in the last 12 months, waking up with chest tightness within the last 12 months, shortness of breath at rest in the last 12 months, shortness of breath after exercise in the last 12 months, woken by attack of shortness of breath in the last 12 months (breathlessness at night), having ever had asthma, attacks of asthma in last 12 months, use of asthma medication, persistent cough, waking up with cough and bringing up phlegm from chest in the morning (4).

BHR and FEV₁ measurements

Bronchial responsiveness to methacholine challenge was measured using the 2-min tidal breathing method. Increasing concentrations of methacholine (0.06, 0.125, 0.25, 0.5, 1, 2, 4, 8 and 16 mg/ml) were aerosolized by a DeVilbiss 646 nebuliser (Sunrise Medical HHG Inc., Somerset, PA, USA) driven by a computer-activated dosimeter (Koko Digidoser System, PDS Instrumentation, Louisville, CO, USA). Forced expiratory volume in the first second (FEV₁) was measured at baseline, and 2 min after each tidal breathing period.

The test was stopped when either a 20% fall in FEV₁ was achieved or the final concentration was reached. The provocative concentration causing a 20% fall in FEV₁ (PC₂₀) was calculated by the Koko software. A positive BHR was defined as PC₂₀ to methacholine challenge of ≤ 8 mg/ml.

Exclusion criteria to a methacholine challenge were conditions that might compromise the quality of the test or might expose the participant to an increased risk or discomfort, such as FEV₁ < 60% predicted, pregnancy, nursing mothers and inability to perform acceptable-quality spirometry. The BHR test was postponed if the participant had respiratory infection, recent smoking or asthma medication (11). We excluded from the analysis 141 subjects out of 2063 because FEV₁ was unsatisfactory or PC₂₀ was missing.

Skin prick test

Skin prick tests (SPT) for allergy were performed for eight extracts of inhalant allergens (*Dermatophagoides pteronyssinus*, *D. farinae*, cat fur, dog hair, *Penicillium notatum*, *Alternaria alternata*, grass pollens and *Aspergillus fumigatus*) together with normal saline as a negative control and histamine (1 mg/ml) as a positive control. A test was considered positive when the mean length and width of the reaction was 3 mm or more (12). Cases with reaction to saline or lack of reaction to histamine were re-scheduled to repeat the test. A 147 subjects had missing data on SPT. The tests and measurements were carried out in the University Hospital, Medical School of Ribeirão Preto, and stringent safety procedures were observed at all times.

Definitions of asthma and asthma score

The asthma score used in the analyses consisted of a sum of the positive answer to the eight questions, i.e. the score ranged from 0 to 8 (1). These questions were chosen from the main factor in a principal component analysis, excluding those questions with a low frequency, a low factor loading or the lowest loading factor among highly correlated questions (1). The items used in this score were: (i) wheeze and breathlessness (positive answer to both questions); (ii) chest tightness; (iii) shortness of breath at rest; (iv) shortness of breath after exercise; (v) woken by attack of shortness of breath; (vi) ever asthma; (vii) attack of asthma and (viii) medication for asthma. Dichotomous definitions of asthma including a positive answer to the question on wheeze, positive answers to wheeze plus awakening with breathlessness, or positive answers to these questions in the absence of a cold. The ECRHS definition of asthma was based on three questions: (i) attack of shortness of breath; (ii) attack of asthma and (iii) use of asthma medication (4).

Known risk factors of asthma

We selected those factors for which there is good evidence of an association with asthma in our data set. These were gender, atopy, maternal and paternal asthma, smoking, perception of food allergy (13), rhinitis, rhino-conjunctivitis and eczema.

Statistical analysis

The three sets of asthma definitions, dichotomous symptoms of asthma, ECRHS questions and the asthma score were compared with positive BHR, positive BHR and atopy, and physician diagnosed asthma in relation to positive and negative likelihood ratios (PLR and NLR) (14). Multiple logistic regression analyses were

carried out to assess the association between risk factors and the dichotomous definitions of asthma. The asthma score was a count from zero to eight positive questions, analysed by a negative binomial generalized linear model (1). When the primary outcome is the number of occurrences, a Poisson distribution is suggested, in which mean and standard deviation (SD) is similar. However, an over-dispersion occurred as the mean was 0.87 and SD was 1.46 thus the use of a negative binomial generalized linear model was required (15). This analysis models the ratio of the mean score among exposed and nonexposed. We confirmed the suitability of the negative binomial over the Poisson distribution by plotting the predicted probabilities according to the observed distribution of positive questions (score) in our data. The risk factors assessed were described above.

Results

The mean age of the 2063 participants was 23.9 years with a SD of 0.7 years, of whom 1068 (51.8%) were women. Current smoking was reported by 17% of the individuals, rhinitis by 58.5%, rhino-conjunctivitis by 24.1% and eczema by 32.2%. Maternal and paternal asthma were reported by 6.9% and 5.4%, respectively. Smoking was more common in men ($P < 0.0001$), but respiratory symptoms and atopic conditions were more common in women, with the exception of asthma and persistent cough. The prevalence of each of the components of the asthma score varied from 3.5% for asthma attacks in the last 12 months, to 18.6%, breathlessness following exercise (Table 1). A positive BHR and atopy were common, 31.3% and 52.1%, respectively.

Table 1. The prevalence of each item of the asthma score, the ECRHS definition and other asthma symptoms, atopy to any allergen, and positive BHR (PC₂₀)

Variables	Percentage (n/M)
<i>Symptoms used in the score</i>	
1. Wheezing and breathlessness (last 12 months)	10.1 (209/2061)
2. Waking up with chest tightness (last 12 months)	12.4 (255/2060)
3. Breathlessness at rest (last 12 months)	12.3 (254/2062)
4. Breathlessness after exercise (last 12 months)	18.6 (378/2037)
5. Breathlessness at night (last 12 months)	9.0 (185/2062)
6. Ever asthma	16.2 (324/1997)
7. Asthma attack (last 12 months)	3.5 (72/2055)
8. Use of medication for asthma	5.8 (119/2063)
<i>ECRHS score</i>	
One positive of three questions	16.4 (338/2063)
Two positives out three questions	3.9 (80/2063)
Three positives out three questions	1.3 (27/2063)
<i>Other symptoms and tests</i>	
Wheezing	19.4 (401/2061)
Wheezing and wakening with breathlessness in the absence of cold (last 12 months)	5.4 (111/2061)
Atopy to any of eight allergens	52.1 (998/1916)
PC ₂₀ ≤ 8 mg/ml	31.3 (601/1922)
Physician diagnosed asthma	7.0 (144/2061)

BHR, bronchial hyperresponsiveness; PC₂₀, provocative concentration causing a 20% fall in FEV₁; FEV₁, forced expiratory volume for first second; ECRHS, European Community Respiratory Health Survey (4).

Positive likelihood ratio were usually higher in relation to physician diagnosed asthma than for positive BHR (Table 2). Positive likelihood ratio increased with asthma scores and ECRHS scores, and was high for wheeze and awakening with breathlessness in the absence of a cold, but the prevalence became too low for useful analysis. The PLR were lower for assessments using the asthma score than for dichotomous assessments or the ECRHS definition. The NLR were too close to 1 in relation to positive BHR, indicating that the absence of asthma symptoms do not predict a negative BHR. Negative likelihood ratio were below 1 in relation to physician diagnosed asthma for wheeze, showing that the absence of wheeze tends to be the main criterion used by physicians in excluding asthma as a diagnosis. More specific definitions of asthma within each of the systems had a higher PLR but the percentage of subjects with characteristics, such as wheeze, awakening with breathlessness in the absence of cold, an asthma score of 4 or over and giving three positive answers using the ECRHS score, were low, 5.3%, 3.5% and 1.3%, respectively. We also used as criterion of validity a positive BHR plus atopy but the PLR and NLR changed only slightly compared with positive BHR only, except for those with two positive answers to the ECRHS definitions.

The PLR in the ECRHS study were well above the PLR in the Brazilian study for all asthma definitions and most options within definitions (Table 3). The NLR were lower in the ECRHS for dichotomous assessments of asthma and for the asthma score, but not for ECRHS definitions.

The ORs of the relationship of each risk factor with wheezing and awakening with breathlessness were higher than with being positive to any one of the ECRHS items (Table 4). Asthma score showed a significant association based on relative change (RC) with maternal asthma and food allergy which were not shown for the other two definitions. The assessment of the asthma scores was based on RCs thus is not directly comparable with ORs.

The prevalence of subjects with each of the risk factors for asthma in Table 4 increased markedly with the score of asthma with the exception of smoking and paternal asthma, but the number of subjects with the higher asthma scores for each risk factor was low, thus having little impact on the total sample estimates.

Discussion

This study has shown that an operational score for asthma and the ECRHS definition had disappointingly low PLR and an NLR slightly below 1 when a positive BHR was used as a relative standard criterion of validity. The highest PLR in relation to a positive BHR was related to wheeze and awakening with breathlessness in

Table 2. PLR and NLR for each system to assess asthma in relation to three gold standards positive atopy, positive BHR and physician diagnosed asthma

Asthma definitions	n	%	BHR* (N = 1922)		BHR* and atopy (N = 1863)		Physician diagnosed asthma (N = 2061)	
			PLR (95% CI)	NLR (95% CI)	PLR (95% CI)	NLR (95% CI)	PLR (95% CI)	NLR (95% CI)
<i>Dichotomous symptoms</i>								
Wheeze	401	19.5	2.46 (2.05; 2.95)	0.78 (0.73; 0.83)	2.40 (2.00; 2.88)	0.75 (0.70; 0.81)	3.18 (2.66; 3.81)	0.55 (0.46; 0.66)
Wheeze and awakening with breathlessness	209	10.1	3.17 (2.41; 4.17)	0.86 (0.82; 0.90)	3.00 (2.29; 3.93)	0.85 (0.81; 0.90)	5.00 (3.88; 6.43)	0.65 (0.57; 0.78)
Wheeze and awakening with breathlessness in the absence of cold	111	5.4	5.50 (3.65; 8.28)	0.91 (0.88; 0.94)	4.67 (3.16; 6.90)	0.89 (0.85; 0.93)	10.33 (7.36; 14.51)	0.71 (0.64; 0.79)
Awakening with chest tightness at night	225	12.4	1.70 (1.33; 2.16)	0.92 (0.88; 0.96)	1.70 (1.31; 2.21)	0.92 (0.86; 0.98)	2.73 (2.07; 3.60)	0.79 (0.71; 0.88)
Awakening with breathlessness at night	185	9.0	1.71 (1.28; 2.28)	0.95 (0.92; 0.98)	1.86 (1.36; 2.54)	0.94 (0.90; 0.98)	4.57 (3.43; 6.09)	0.73 (0.65; 0.82)
<i>ECRHS definition</i>								
One of three	338	16.4	2.00 (1.63; 2.45)	0.86 (0.81; 0.90)	2.00 (1.62; 2.47)	0.85 (0.80; 0.90)	3.57 (2.93; 4.35)	0.58 (0.71; 0.99)
Two of three	80	3.9	2.67 (2.04; 3.49)	0.95 (0.93; 0.97)	10.00 (5.96; 16.77)	0.91 (0.88; 0.94)	16.00 (10.63; 24.09)	0.69 (0.62; 0.77)
Three of three	27	1.3	—	0.96 (0.94; 0.98)	—	0.96 (0.94; 0.98)	—	0.86 (0.81; 0.92)
<i>Asthma Score</i>								
One of eight	405	19.6	1.47 (1.22; 1.77)	0.90 (0.85; 0.95)	1.44 (1.18; 1.76)	0.90 (0.84; 0.96)	1.53 (1.17; 2.01)	0.87 (0.78; 0.97)
Two or three of eight	167	8.1	1.57 (1.16; 2.12)	0.96 (0.93; 0.99)	1.71 (1.24; 2.37)	0.95 (0.91; 0.99)	2.00 (1.33; 3.0)	0.91 (0.84; 0.98)
Four to eight of eight	72	3.5	2.00 (1.25; 3.19)	0.96 (0.93; 0.98)	2.33 (1.44; 3.76)	0.96 (0.93; 0.99)	3.67 (2.16; 6.23)	0.92 (0.86; 0.98)

PLR, positive likelihood ratio; NLR, negative likelihood ratio; ECRHS, European Community Respiratory Health Survey; BHR, bronchial hyperresponsiveness.

* PC₂₀ ≤ 8 mg/ml (4).

Table 3. PLR and NLR of the three operational definitions of asthma in comparison to positive BHR in the ECRHS and Brazilian studies

	PLR		NLR	
	ECRHS	Brazil	ECRHS	Brazil
<i>Wheeze</i>				
Wheeze	2.61	2.46	0.64	0.78
Wheeze and awakening with breathlessness	4.43	3.17	0.74	0.86
Wheeze and awakening with breathlessness in the absence of cold	4.80	5.50	0.80	0.91
<i>ECRHS definition</i>				
Any one of three variables	5.00	2.00	0.79	0.58
Any two of three variables	14.00	2.67	0.87	0.69
Any three of three variables	Undetermined	Undetermined	0.94	0.86
<i>Score</i>				
Any one of eight questions	2.07	1.47	0.56	0.87
Any two of eight questions	3.64	1.57	0.67	0.96
Any three of eight questions	5.60	3.00	0.76	0.96
Any four of eight questions	10.00	3.00	0.82	0.98
Any five of eight questions	15.00	3.00	0.86	0.98
Any six of eight questions	11.00	Undetermined	0.90	0.99
Any seven of eight questions	Undetermined	Undetermined	0.94	0.98
All eight questions	Undetermined	Undetermined	0.98	0.99

PLR, positive likelihood ratio; NLR, negative likelihood ratio; BHR, bronchial responsiveness.

Definition of positive BHR in the ECRHS study is a 20% fall in FEV₁ at 1 mg.

Definition of positive BHR in the Brazilian study is a 20% fall in FEV₁ at 8 mg/ml

Undetermined as denominators were equal to zero. European Community Respiratory Health Survey (ECRHS) data from Ref. 1.

the absence of a cold. The PLR in relation to BHR in this Brazilian study were, for most asthma definitions, lower than in the ECRHS study (1). The PLR was higher and

the NLR further below from 1 for physician diagnosed asthma in comparison with other standard criteria used. This would indicate that doctors may have relied mainly on symptoms when deciding a diagnosis of asthma. The PLR increased negligibly when positive BHR was combined with atopy.

This study group has several characteristics worth mentioning in contrast to the ECRHS study. The prevalence of asthma symptoms was well below the levels reported in the ECRHS study, but the prevalence of atopy and positive BHR were high. Our measure of BHR was based on methacholine concentration, while the ECRHS study was based on methacholine dose. These two approaches cannot be directly compared, but they have been reported to be equivalent (16). The prevalence of smoking in Brazil is unusually low. There is clear evidence that Brazil has not experienced the trend of increasing tobacco consumption seen in many developing countries (17). Thus, the community attributable risk of smoking to respiratory symptoms should be low in comparison with ECRHS centres. This could be considered an advantage in our study because the chance of participants having symptoms because of progression towards chronic obstructive lung disease should be lower than in the ECRHS study.

Although a continuous score to diagnose asthma is attractive, one of the problems with its use would be the low percentage of individuals in the population with a score above 3. In our study, 3.5% of the participants had a score of 4 or over, but in the ECRHS this percentage was 11.1% (1). Thus, in many populations, including the Brazilian population, the advantage of using an asthma score would be lost by the clustering of subjects in the lower scores of the scale. In our analysis, we merged the

Table 4. Association between risk factors of asthma and the three operational definitions of asthma. OR and RC are adjusted for all the variables in the table

Variable (n/N)	Wheezing and breathlessness		ECRHS definition*		Asthma score	
	OR	CI (95%)	OR	CI (95%)	RC	CI (95%)
Atopy (998/1916)	2.23	(1.47; 3.38)	1.47	(1.08; 1.99)	1.77	(1.49; 2.10)
Smoking (533/2063)	2.23	(1.50; 3.30)	1.52	(1.09; 2.11)	1.35	(1.13; 1.63)
Females (1068/2063)	1.55	(1.04; 2.29)	2.65	(1.92; 3.65)	1.74	(1.46; 2.06)
Maternal asthma (128/1863)	1.54	(0.81; 2.92)	1.58	(0.93; 2.68)	1.67	(1.24; 2.25)
Paternal asthma (91/1696)	1.21	(0.60; 2.43)	0.93	(0.50; 1.71)	1.10	(0.79; 1.54)
Food allergy (179/2048)	1.54	(0.88; 2.68)	1.08	(0.66; 1.76)	1.31	(1.00; 1.71)
Rhinitis (1206/2063)	2.63	(1.54; 4.49)	2.46	(1.68; 3.60)	1.79	(1.47; 2.18)
Rhino-conjunctivitis (494/2048)	2.12	(1.40; 3.21)	1.59	(1.14; 2.23)	1.38	(1.13; 1.68)
Eczema (664/2063)	1.08	(0.73; 1.60)	1.10	(0.81; 1.50)	1.09	(0.91; 1.29)

OR, Odds ratios; RC, relative change.

* Any one of three. ECRHS: European Community Respiratory Health Survey (4)

groups with higher score into one group. A similar problem was observed in relation to the ECRHS definition of asthma because attacks of asthma in the last 12 months and use of asthma medication were infrequently reported. The inclusion of asthma treatment as a criterion of asthma is problematic because it is highly dependent on the standard and structure of health services (18). In Latin America the standard may be patchy, especially in rural areas, and a large proportion of the population may not be prescribed appropriate treatment (19).

It could be argued that the use of asthma score would be supported by the lack of a threshold between asthma score and the main risk factors of asthma, and the use of the score would increase the statistical power to detect associations with risk factors (1, 20). In our study, there was some support for such a view as maternal asthma and perceived food allergy were related to the asthma score but they were not associated with dichotomous variables or the ECRHS definitions. None of the definitions of asthma were associated with eczema, probably because, we suspect, of a high frequency of misclassification. The ECRHS question 'Have you ever had eczema or another type of skin allergy?' may have been misunderstood by many participants in our study. The questions about parental asthma and food allergy may have also been subject to a high level of misclassification as participants may be unaware of their parents' asthma status and the concept of IgE-mediated reaction to food would have been misunderstood by many (13).

In the current study there were some combinations of symptoms, such as wheeze and awakening with breathlessness at night in the absence of cold that increased the PLR. As the frequency of such a combination was relatively low (5.3%), the problem of its use would have similar drawbacks to the use of asthma scores.

An explanation for the lower PLR in our study than that reported in the ECRHS study is that our study did

not contribute to the analysis to develop the asthma score while Pekkanen et al. analysed the same data used for developing their asthma score, performing a principal components analysis (1). The strength of our analysis is that our sample is independent of the study used to build the asthma score. It is also important to highlight that the use of data published in a Chilean study did not show a higher PLR than the results shown in this Brazilian study (19). Sunyer et al. (18) argued, based on a factor analysis, that the ECRHS questionnaire demonstrated great internal consistency between participating countries. However, they found that Spain and, to a lesser extent, other participant countries departed from the more restricted factor structure in their analysis. We endorse their suggestion that issues relating to differences in the use of the term asthma may create cross-cultural confusion, given the variety of approaches between countries in relation to the functioning of health services and doctors' diagnostic and management behaviour (18).

A limitation of our study is that we did not formally study the reproducibility of the ECRHS questionnaire in a Brazilian population. However, the ISAAC questionnaire translation has been assessed for agreement of answers over a period of 4 weeks, and high Kappa values were found (21). We used, as far as possible, similar expressions to translate ECRHS questions into Portuguese.

The PLR increased with asthma scores, but the prevalence became too low for any useful analysis. These data are helpful in highlighting that if a majority of participants in a study tend to cluster in low asthma scores, the benefit of using asthma scores would be only marginal. It is possible that the use of asthma scores is helpful when used in populations where the frequency of participants with high asthma scores is high. There was no advantage in using asthma scores instead of dichotomous variables or the ECRHS definition in relation to

PLR. There were marginal benefits in using asthma scores to assess risk factors of asthma. As the PLR were disappointingly low when positive BHR was used to assess relative validity in our study, it would be helpful to repeat the principal components analysis in independent ECRHS samples to explore the robustness of other asthma scores.

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